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Authors' Reply

Michael Bracken raised concerns about our umbrella review and meta-analysis, regarding two of the included studies: Andalib et al.[1] and Morales et al.[2].[3] Both meta-analyses tested the association of antidepressant use - vs unexposed groups and autism spectrum disorder, but Morales et al[2] addressed the overall association of antidepressant use (including SSRIs but without providing a subset of analysis of SSRIs) vs unexposed, while Andalib et al[1] addressed the specific association of SSRI use (not the other antidepressants) vs unexposed. To ensure that all the exposures analysed in our umbrella review were as specific as possible, we included Andalib et al[1] and not Morales et al[2]. Morales et al.[2], was rather included to assess the association between prepregnancy exposure to antidepressant use and autism spectrum disorder.

Bracken highlighted potential intrinsic errors within the meta-analysis of Andalib et al.[1]. As we have acknowledged in the limitation paragraph of our study[3], re-assessing primary errors in 119 eligible meta-analyses and their individual studies is out of the scope of umbrella reviews.[4] We have re-analysed Andalib et al[1] results after correcting for the biases highlighted by Bracken and found that the summary estimate was still statistically significant (OR 1.57, 95% CI 1.19 to 2.07). We have also re-analyzed the association of antidepressant use vs unexposed and autism spectrum disorder reported by Morales et al[2] (digitally extracting data from their[2] figure 2 -a procedure which was not originally planned in our protocol). The results were similarly graded as convincing evidence according to the established criteria (n of studies=11, OR 1.53, 95% CI 1.31 to 1.78, p=0.000000041, I^2=33, 95% prediction interval 1.07 to 2.19, Egger p=0.82, no signs of biases). Therefore there are no changes in the direction of our results.

Certainly, the association of SSRI use vs unexposed and autism spectrum disorder is likely due to confounding, as we acknowledged (p.597) [3]. We concluded that overall, our findings suggest that maternal psychiatric disorder might act as an independent risk factor for autism spectrum disorder[3]. Therefore, there are no errors in the interpretation of our results.

All authors declare no competing interests.

Jong Yeob Kim[1], Paolo Fusar-Poli[2,3,4], Jae Il Shin[5*]

1. Yonsei University College of Medicine, Seoul, Republic of Korea.
2. Early Psychosis: Interventions and Clinical-detection (EPIC) lab, Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom.

3. OASIS service, South London and Maudsley NHS Foundation Trust, London, United Kingdom.
4. Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy.
5. Department of Pediatrics, Yonsei University College of Medicine, Seoul, Republic of Korea.

*Corresponding Author:

Prof. Jae Il Shin, MD, PhD.

Yonsei-ro 50, Seodaemun-gu, C.P.O. Box 8044, Department of Pediatrics, Yonsei University College of Medicine, Seoul 120-752, Korea

E-mail: shinji@yuhs.ac

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